REMARKS

In paper number 18, the Office Action mailed on November 14, 2002, the Examiner communicated a number of rejections. Claims 1, 3-10, 17 and 19-25 were at issue. Claims 1, 3-10, 17 and 19-25 were rejected. The Examiner made the following rejections:

(1) Claims 1, 3-10, 17, and 19-25 were rejected under 35 U.S.C. 112 (second paragraph).

(2) Claim 20 was objected to, under 37 CFR §1.75, as substantially duplicative of claim 7.

Applicants believe the present amendments, and the following remarks, traverse the Examiner's rejection of the claims. These remarks are presented in the same order as they appear above.

1. The Claims Are Definite

The Examiner rejects claims 1, 3-10, 17 and 19-25 under 35 U.S.C. 112, second paragraph. Specifically the Examiner alleges that,

> "[c]laims 1 and 17 are vague and indefinite for recitation 'under conditions such that said second brain tissue sample is evaluated for anatomical changes consistent with a diagnosis of multiple sclerosis.' It is not clear, first, what is encompassed by the 'conditions' for comparing the degree of binding."[1]

Once again, the Examiner is reminded that "[c]laims of a patent application *are to be construed in the light of the specification* and the understanding thereof by those skilled in that art to whom they are addressed'." *Application of Salem*, 553 F.2d 676, 683, 193 USPQ 513 (CCPA 1977) (quoting *In re Myers*, 410 F.2d 420, 425 (CCPA 1969) with emphasis added in *Salem*). Furthermore, "[i]f the claims, read in the light of the specifications, reasonably apprise those skilled in the art both of the utilization and scope of the invention, and if the language is as precise as the subject matter permits, the courts can demand no

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[1] Office Action mailed November 14, 2002, p.3.

more." *Georgia-Pacific Corp. v. United States Plywood Corp.*, 258 F.2d 124, 136, 118 USPQ 122, 132 (2d Cir.), *cert. denied*, 358 U.S. 884 (1958).

In view of this well settled case law, Applicants assert that the "conditions" for "comparing the degree of binding" are perfectly definite when these claim terms are read in view of the specification of the application as filed. However, in order to further their business interests and without acquiescing to the Examiner's arguments, while expressly reserving the right to prosecute the claims as originally filed (or claims similar thereto), the Applicants have amended, independent, claims 1 and 17.

Applicants have replaced the phase, "under conditions such that said second brain tissue sample is evaluated for anatomical changes consistent with a diagnosis of multiple sclerosis" with "wherein a difference in said binding confirms the detection of multiple sclerosis in said first tissue sample." This amendment highlights an important feature of the claimed embodiments of the present invention. Specifically, this amendment emphasizes that *any difference* in the degree of binding of iron binding protein to, i) the first brain tissue sample[2] (e.g. the experimental sample) and ii) the second brain tissue sample (e.g. the control) is diagnostic of multiple sclerosis in said first tissue sample.

It is important to stress that any difference in binding of iron binding protein (between the first and second samples) is diagnostic. As noted in the specification of the application as filed, different iron binding proteins bind differently to, i) brain tissue from a human suspected of having a demyelinating disease and ii) brain tissue from a human free of the pathological manifestations of a demyelinating disease. For example, the Applicants use *the lack of ferritin binding* observed in CNS lesions and periplaque margins as a means to detect

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[2] Applicants have further amended claims 1 and 17 such that, in step "c", a difference in iron binding confirms the detection of multiple sclerosis in the *first* brain tissue sample (e.g. tissue from a human suspected of having a demyelinating disease).

demyelinating disease. While it is not intended that the present invention be limited to any one iron binding protein or binding mechanism, in one embodiment the Applicants teach that,

> "ferritin binding is absent within the lesion itself which suggests ferritin is not binding to microglia or astrocytes; the two other types of glial cells found in white matter and which heavily populate the lesion."[3]
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> * * *
>
> "[t]herefore the present invention contemplates assay systems which are based on the differential binding of ferritin in normal brains and the brains of persons afflicted with MS. In a preferred embodiment, immunocytochemical methods are used identify demyelinated lesions in the brain (consistent with a finding of MS) which substantially fail to bind ferritin."[4]

Conversely, the Applicants use *the binding of transferrin* in periplaque regions as another means to detect demyelinating disease. Specifically, the Applicants teach that:

> "the normal distributions of transferrin and ferritin binding sites are altered in and around plaques from periventricular white matter isolated from multiple sclerotic (MS) brains. In direct contrast to ferritin binding, transferrin binding in the MS tissue can be seen in white matter periplaque regions and to varying degrees within the lesion itself."[5]

The Applicants teach the relative binding of iron binding proteins as an index to differentially detect pathologies consistent with demyelinating disease (including MS) in a sample from a human suspected of having a demyelinating disease. That is to say, the specification correlates the degree of binding between a human tissue sample and a specific iron binding protein to the detection of a demyelinating disease in a tissue. Therefore, the Applicants submit that (in view of the teaching provided by the Specification) it is *not necessary* to categorically recite, in the claims, whether said binding is either increased or decreased. As discussed above, the relative degree of binding (or lack thereof) is specific to a given iron binding protein. Therefore *any difference in binding*, between the first (e.g. experimental) tissue sample and the second (e.g. control) sample, and a given iron binding protein, confirms the detection of multiple sclerosis in said first tissue sample. In this respect, the Applicants particularly point out and distinctly claim the subject matter which they regard as their invention. The Applicants, therefore, respectfully request the Examiner withdraw the

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[3] Application as filed, p. 8, ll. 14-16.

[4] *Id.* at p. 8, ll. 22-25.

[5] *Id* at, p. 8, ll. 6-10.

pending rejections, under 35 U.S.C. § 112 (second paragraph), of independent claims 1 and 17 (and claims dependent thereon).

2. Applicants Cancel, Without Prejudice, Claims 20, 21, and 22

The Examiner asserts that,

> "should claim 7 be found allowable, claim 20 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k)."

In order to further their business interests and without acquiescing to the Examiner's arguments, while expressly reserving the right to prosecute the claims as originally filed (or claims similar thereto), the Applicants have cancelled claims 20, 21, and 22.

CONCLUSION

The Applicants believe the arguments and claim amendments set forth above traverse the Examiner's rejections and, therefore, request that all grounds for rejection be withdrawn for the reasons set out above. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, the Applicants encourage the Examiner to call the undersigned collect at 617.252.3353.

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APPENDIX I
MARKED-UP VERSION OF REWRITTEN CLAIMS
PURSUANT TO 37 CFR § 1.121 (c)(1)(ii)

The following rewritten claims were amended as follows:

1. A method for the detection of multiple sclerosis comprising:

   a) providing: i) a first brain tissue sample from a human suspected of having a demyelinating disease, ii) a second brain tissue sample from a human free from the pathological manifestations of a demyelinating disease, and iii) iron binding protein;

   b) reacting, in vitro, said first and second brain tissue samples with said iron binding protein; and

   c) comparing the degree of binding of said iron binding protein with said first and second brain tissue samples [under conditions such that said second brain tissue sample is evaluated for anatomical changes consistent with a diagnosis of multiple sclerosis] <u>wherein a difference in said binding confirms the detection of multiple sclerosis in said first tissue sample.</u>

17. A method for the detection of multiple sclerosis comprising:

   a) providing: i) a first brain tissue sample from a human suspected of having a demyelinating disease, ii) a second brain tissue sample from a human free from the pathological manifestations of a demyelinating disease, and iii) iron binding protein wherein said iron binding protein is linked to a detectable marker;

   b) reacting, in vitro, said first and second brain tissue samples with said iron binding protein; and

c) comparing the degree of binding of said iron binding protein with said first and second brain tissue samples [under conditions such that said second brain tissue sample is evaluated for anatomical changes consistent with a diagnosis of multiple sclerosis] wherein a difference in said binding confirms the detection of multiple sclerosis in said first tissue sample.

APPENDIX II
CLEAN VERSION OF THE ENTIRE SET OF PENDING CLAIMS PURSUANT TO 37 CFR § 1.121 (c)(3)

1. A method for the detection of multiple sclerosis comprising:

   a) providing: i) a first brain tissue sample from a human suspected of having a demyelinating disease, ii) a second brain tissue sample from a human free from the pathological manifestations of a demyelinating disease, and iii) iron binding protein;

   b) reacting, in vitro, said first and second brain tissue samples with said iron binding protein; and

   c) comparing the degree of binding of said iron binding protein with said first and second brain tissue samples wherein a difference in said binding confirms the detection of multiple sclerosis in said first tissue sample.

3. The method of Claim 1, wherein said brain tissue is collected *via* surgical biopsy.

4. The method of Claim 1, wherein said iron binding protein is ferritin.

5. The method of Claim 4, wherein said ferritin is native.

6. The method of Claim 4, wherein said ferritin is recombinant.

7. The method of Claim 4, wherein said ferritin is linked to a detectable marker.

8. The method of Claim 7, wherein said marker is selected from the group consisting of radioisotope and fluorescent dye.

9. The method of Claim 8, wherein said radioisotope is ^{125}I.

10. The method of Claim 1, wherein said measuring is performed with a technique selected from the group of autoradiography and immunofluorescence.

17. A method for the detection of multiple sclerosis comprising:

a) providing: i) a first brain tissue sample from a human suspected of having a demyelinating disease, ii) a second brain tissue sample from a human free from the pathological manifestations of a demyelinating disease, and iii) iron binding protein wherein said iron binding protein is linked to a detectable marker;

b) reacting, in vitro, said first and second brain tissue samples with said iron binding protein; and

c) comparing the degree of binding of said iron binding protein with said first and second brain tissue samples wherein a difference in said binding confirms the detection of multiple sclerosis in said first tissue sample.

19. The method of Claim 17, wherein said brain tissue is collected *via* surgical biopsy.

23. The method of Claim 17, wherein said marker is selected from the group consisting of radioisotope and florescent dye.

24. The method of Claim 23, wherein said radioisotope is ^{125}I.

25. The method of Claim 17, wherein said measuring is performed with a technique selected from the group of autoradiography and immunofluorescence.